



#4

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<120> MODIFICATIONS OF THE VEGF RECEPTOR-2 PROTEIN AND  
METHODS OF USE

<130> 0125-0016US

<140> 09/390,326

<141> 1999-09-07

<160> 12

<170> PatentIn Ver. 2.0

<210> 1

<211> 31

<212> DNA

<213> Homo sapiens

<400> 1

cagcatatgg atccagatga actcccattg g

31

<210> 2

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<212> DNA

<213> Homo sapiens

<400> 2

gcggtcgact taaacaggag gagagctcag tgtg

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<211> 33

<212> DNA

<213> Homo sapiens

<400> 3

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<210> 4

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<212> DNA

<213> Homo sapiens

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cctgtcgact tatccagaat cctcttccat gctcaaag

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<400> 5

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 Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly  
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 Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala  
 35 40 45  
 Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met  
 50 55 60  
 Leu Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu  
 65 70 75 80  
 Leu Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu  
 85 90 95  
 Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu  
 100 105 110  
 Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn  
 115 120 125  
 Glu Phe Val Pro Tyr Lys Glu Ala Pro Glu Asp Leu Tyr Lys Asp Phe  
 130 135 140  
 Leu Thr Leu Glu His Leu Leu Ile Cys Tyr Ser Phe Gln Val Ala Lys  
 145 150 155 160  
 Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala  
 165 170 175  
 Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile Cys Asp  
 180 185 190  
 Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys  
 195 200 205  
 Gly Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr Ile Phe  
 210 215 220  
 Asp Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly Val Leu  
 225 230 235 240  
 Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Lys  
 245 250 255  
 Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg Met Arg  
 260 265 270

Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys  
 275. 280 285

Trp His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu  
 290 295 300

His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp  
 305 310 315

<210> 6

<211> 386

<212> PRT

<213> E. coli

<400> 6

Asp Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp  
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Gly Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val  
 20 25 30

Val Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys  
 35 40 45

Val Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln  
 50 55 60

Ala Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu  
 65 70 75 80

Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr  
 85 90 95

Ile Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His  
 100 105 110

Lys Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys  
 115 120 125

Glu Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser  
 130 135 140

Tyr Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys  
 145 150 155 160

Gln Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val  
 165 170 175

Ser Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser  
 180 185 190

Tyr Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser  
 195 200 205

Asp Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr  
 210 215 220

Tyr Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val  
 225 230 235 240

His Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile  
 245 250 255

Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser  
 260 265 270

Asn Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala  
 275 280 285

Pro Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp  
 290 295 300

Ser Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro  
 305 310 315 320

Tyr Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser  
 325 330 335

Gly Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu  
 340 345 350

Ile Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe  
 355 360 365

Tyr His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys  
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Lys Ser  
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<210> 7

<211> 310

<212> PRT

<213> Homo sapiens

<400> 7

Met Leu Ala Gly Val Ser Glu Tyr Glu Leu Pro Glu Asp Pro Arg Trp  
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Glu Leu Pro Arg Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly  
 20 25 30

Cys Phe Gly Gln Val Val Leu Ala Glu Ala Ile Gly Leu Asp Lys Asp  
 35 40 45

Lys Pro Asn Arg Val Thr Lys Val Ala Val Lys Met Leu Lys Ser Asp  
 50 55 60

Ala Thr Glu Lys Asp Leu Ser Asp Leu Ile Ser Glu Met Glu Met Met  
 65 70 75 80

Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys  
 85 90 95

Thr Gln Asp Gly Pro Leu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly  
 100 105 110  
 Asn Leu Arg Glu Tyr Leu Gln Ala Arg Arg Pro Pro Gly Leu Glu Tyr  
 115 120 125  
 Cys Tyr Asn Pro Ser His Asn Pro Glu Glu Gln Leu Ser Ser Lys Asp  
 130 135 140  
 Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu Ala  
 145 150 155 160  
 Ser Lys Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu Val  
 165 170 175  
 Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp  
 180 185 190  
 Ile His His Ile Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro  
 195 200 205  
 Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Ile Tyr Thr His  
 210 215 220  
 Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Thr  
 225 230 235 240  
 Leu Gly Gly Ser Pro Tyr Pro Gly Val Pro Val Glu Glu Leu Phe Lys  
 245 250 255  
 Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ser Asn Cys Thr Asn  
 260 265 270  
 Glu Leu Tyr Met Met Met Arg Asp Cys Trp His Ala Val Pro Ser Gln  
 275 280 285  
 Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Ile Val Ala  
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 Leu Thr Ser Asn Gln Glu  
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<210> 8

<211> 297

<212> PRT

<213> Homo sapiens

<400> 8

Val Phe Pro Cys Ser Val Tyr Val Pro Asp Glu Trp Glu Val Ser Arg  
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 20 25 30  
 Val Tyr Glu Gly Asn Ala Arg Asp Ile Ile Lys Gly Glu Ala Glu Thr  
 35 40 45

Arg Val Ala Val Lys Thr Val Asn Glu Ser Ala Ser Leu Arg Glu Arg  
 50 55 60  
 Ile Glu Phe Leu Asn Glu Ala Ser Val Met Lys Gly Phe Thr Cys His  
 65 70 75 80  
 His Val Val Arg Leu Leu Gly Val Val Ser Lys Gly Gln Pro Thr Leu  
 85 90 95  
 Val Val Met Glu Leu Met Ala His Gly Asp Leu Lys Ser Tyr Leu Arg  
 100 105 110  
 Ser Leu Arg Pro Glu Ala Glu Asn Asn Pro Gly Arg Pro Pro Pro Thr  
 115 120 125  
 Leu Gln Glu Met Ile Gln Met Ala Ala Glu Ile Ala Asp Gly Met Ala  
 130 135 140  
 Tyr Leu Asn Ala Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn  
 145 150 155 160  
 Cys Met Val Ala His Asp Phe Thr Val Lys Ile Gly Asp Phe Gly Met  
 165 170 175  
 Thr Arg Asp Ile Tyr Glu Thr Asp Tyr Tyr Arg Lys Gly Gly Lys Gly  
 180 185 190  
 Leu Leu Pro Val Arg Trp Met Ala Pro Glu Ser Leu Lys Asp Gly Val  
 195 200 205  
 Phe Thr Thr Ser Ser Asp Met Trp Ser Phe Gly Val Val Leu Trp Glu  
 210 215 220  
 Ile Thr Ser Leu Ala Glu Gln Pro Tyr Gln Gly Leu Ser Asn Glu Gln  
 225 230 235 240  
 Val Leu Lys Phe Val Met Asp Gly Gly Tyr Leu Asp Gln Pro Asp Asn  
 245 250 255  
 Cys Pro Glu Arg Val Thr Asp Leu Met Arg Met Cys Trp Gln Phe Asn  
 260 265 270  
 Pro Asn Met Arg Pro Thr Phe Leu Glu Ile Val Asn Leu Leu Lys Asp  
 275 280 285  
 Asp Leu His Pro Ser Phe Pro Glu Val  
 290 295

<210> 9

<211> 367

<212> PRT

<213> Homo sapiens

<400> 9

Met Asp Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro  
 1 5 10 15

Tyr Asp Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly  
 20 25 30  
 Lys Ser Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala  
 35 40 45  
 Phe Gly Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met  
 50 55 60  
 Leu Lys Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu  
 65 70 75 80  
 Leu Lys Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu  
 85 90 95  
 Leu Gly Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu  
 100 105 110  
 Tyr Cys Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp  
 115 120 125  
 Leu Phe Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys  
 130 135 140  
 Glu Lys Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp  
 145 150 155 160  
 Ser Val Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp  
 165 170 175  
 Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr  
 180 185 190  
 Lys Glu Pro Ile Thr Met Glu Asp Leu Ile Ser Tyr Ser Phe Gln Val  
 195 200 205  
 Ala Arg Gly Met Glu Phe Leu Ser Ser Arg Lys Cys Ile His Arg Asp  
 210 215 220  
 Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Asn Asn Val Val Lys Ile  
 225 230 235 240  
 Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asn Pro Asp Tyr Val  
 245 250 255  
 Arg Lys Gly Asp Thr Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser  
 260 265 270  
 Ile Phe Asp Lys Ile Tyr Ser Thr Lys Ser Asp Val Trp Ser Tyr Gly  
 275 280 285  
 Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Ser Pro Tyr Pro Gly  
 290 295 300  
 Val Gln Met Asp Glu Asp Phe Cys Ser Arg Leu Arg Glu Gly Met Arg  
 305 310 315 320

Met Arg Ala Pro Glu Tyr Ser Thr Pro Glu Ile Tyr Gln Ile Met Leu  
 325 330 335

Asp Cys Trp His Arg Asp Pro Lys Glu Arg Pro Arg Phe Ala Glu Leu  
 340 345 350

Val Glu Lys Leu Gly Asp Leu Leu Gln Ala Asn Val Gln Gln Asp  
 355 360 365

<210> 10  
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 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Oligonucleotide

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<210> 11  
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 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Oligonucleotide

<400> 11  
 gaatttgccc cctacaagga agctcctgaa gatctg

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<210> 12  
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 <212> PRT  
 <213> Homo sapiens

<400> 12  
 Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His Cys Glu Arg Leu Pro  
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Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly  
 20 25 30

Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala  
 35 40 45

Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met  
 50 55 60

Leu Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu  
 65 70 75 80

Leu Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu  
 85 90 95



Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu  
 100 105 110

Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn  
 115 120 125

Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg Phe Arg Gln Gly Lys  
 130 135 140

Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys Arg Arg Leu Asp Ser  
 145 150 155 160

Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly Phe Val Glu Glu Lys  
 165 170 175

Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro Glu Asp Leu Tyr Lys  
 180 185 190

Asp Phe Leu Thr Leu Glu His Leu Leu Ile Cys Tyr Ser Phe Gln Val  
 195 200 205

Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp  
 210 215 220

Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile  
 225 230 235 240

Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val  
 245 250 255

Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr  
 260 265 270

Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly  
 275 280 285

Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly  
 290 295 300

Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg  
 305 310 315 320

Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu  
 325 330 335

Asp Cys Trp His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu  
 340 345 350

Val Glu His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp  
 355 360 365